CASE REPORT

Labour outcomes in siblings with channelopathy associated insensitivity to pain due to bi-alleleic SCN9A mutations

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Summary: The gene SCN9A encodes for the voltage-gated sodium channel Nav1.7, which is highly expressed in pain sensing neurons. Bi-allelic 'loss of function' mutations result in a channelopathy associated with insensitivity to pain and anosmia. This is the first report of the labour and postpartum outcomes of two sisters who belong to a non-consanguineous Caucasian family with homozygous SCN9A mutations. Neither sister experienced pain during labour; this had major implications for the staff titrating the syntocinon for labour augmentation and contributed towards their ultimate delivery by caesarean section. During the postpartum period, one of the sisters developed lower limb sensory loss and investigations revealed a spinal haematoma and unrecognized bilateral pelvic fractures. The other sister had an uneventful recovery and both babies are well. These case histories underline the importance of pain in labour management and its function in alerting patients and staff to problems during the puerperium.

Keywords: high-risk pregnancy, *SCN9A*, channelopathy associated insensitivity to pain

INTRODUCTION

The ability to experience pain is of fundamental importance to all animals; it protects individuals from harm and evokes behaviours that promote tissue healing.[1,2] The pain associated with labour protects the mother from damage, in particular to the axial skeleton and bladder. The gene *SCN9A*, encodes for the α-subunit of the voltage gated sodium channel $Na_v1.7$, which is highly expressed in nociceptive neurons and necessary for nociception[1–3] and also essential for odour perception in olfactory sensory neorones.[4] Bi-allelic 'non-sense' mutations (prematurely truncated proteins) in *SCN9A* lead to a lifelong inability to experience acute pain[3] and anosmia.[4] This report presents the labour outcomes of two affected individuals who had been identified as carrying the mutation before pregnancy during studies on a cohort of patients with insensitivity to pain.

CASE 1

A 31-year-old primigravida with bi-allele mutation of *SCN9A* booked at nine weeks gestation. She had experienced multiple injuries in the past, many of which had been unreported or overlooked, including a corneal abrasion resulting in partial blindness.

She had an uneventful pregnancy but presented with pre-labour rupture of membranes at 38 weeks. The admission cardiotocography (CTG) showed irregular uterine activity of which she was unaware. She received 1 mg prostaglandin E2 followed by syntocinon augmentation. During her labour she continued to experience no pain. The syntocinon was titrated with difficulty against her CTG-recorded contractions and reached the maximal dose permitted for primigravida. The labour was complicated by uterine overstimulation. Review at 11 hours showed cervical dilation of 3 cm and a suspicious CTG; she progressed to category 2 caesarean section. This was carried out under routine spinal anaesthetic with bupivacaine and diamorphine. Despite reporting no postoperative pain she was given regular paracetamol and ibuprofen and offered codeine phosphate as required. The patient was discharged ostensibly well at 48 hours with daily community midwife visits.

Seven weeks post caesarean section, she re-presented with groin 'discomfort', saddle anaesthesia and an inability to defaecate or micturate. Examination demonstrated sensory loss in the lower limbs, absent ankle reflexes and reduced anal tone. A magnetic resonance imaging scan revealed para-sacral and pubic rami fractures with callus formation, and a spinal haematoma, which were managed conservatively. Bone-density scanning demonstrated osteoporosis. She was given calcium/vitamin D supplementation and discharged 41 days later, still with a disturbed gait but improving sensation. The patient was advised to have a pregnancy interval of at least two years.

CASE 2

The 35-year-old primigravida sister of the above patient also with a known bi-allelic mutation of *SCN9A* booked at seven weeks gestation. As a child, she had sustained multiple fractures to both lower limbs. She experienced 'flu-like' symptoms not only to 'flu, but to noxious stimuli instead of pain. A bone density scan at 27 weeks gestation was performed as a

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consequence of her sibling's osteoporotic fractures and was reported as normal.

She had an uneventful antenatal period and presented at 40 weeks gestation with pre-labour rupture of membranes and meconium stained liquor. She was aware of contractions but did not find them painful. Her labour was augmented with syntocinon but titration was difficult reaching only two-thirds of the permissible primigravida dose. Due to slow progress of labour she was delivered by category 2 caesarean section under routine spinal anaesthesia. Postoperatively, she received regular paracetamol and diclofenac and she made a good postoperative recovery. A pelvic radiograph showed no pelvic fractures. She and her baby were discharged fit and well two days later.

DISCUSSION

Channelopathy associated insensitivity to pain (CIP) is associated with anosmia but an otherwise normal peripheral and central nervous system.[2] It should not be confused with congenital insensitivity to pain with anhydrosis (CIPA), which is associated with anhydrosis, insensitivity to pain, episodes of hyperpyrexia and loss of nociceptive afferent neurons.[1,2,5] There is no literature regarding CIP and pregnancy.

The value of pain in labour is clearly highlighted by these cases. In the first patient, although the indication for a caesarean section was for fetal compromise, there was also evidence of failure to progress. However, in both cases the lack of pain made it impossible to gauge the true strength of the contractions, which made it difficult to titrate the syntocinon.

Additionally there is no literature regarding CIP and anaesthesia and both our women received routine spinal anaesthesia and postoperative analgesia although neither complained of any pain.

Osteoporosis of pregnancy is not associated with CIP. However, our first patient's inability to experience pain prevented awareness of the fractured pelvis, and delayed her seeking medical help. She now has a persistently altered bony pelvis and gait abnormality, which preclude further vaginal deliveries.

The spinal haematoma was discovered when the patient presented with neurological symptoms. Vertebral column haematoma can occur spontaneously and also as a rare complication of regional anaesthesia although usually this is associated with epidural anaesthesia for postoperative pain in the elderly on LMW heparin prophylaxis; paraplegia can result if diagnosis and treatment is delayed.[6] Classical symptoms include intense back pain and neurological deficit in the legs.[6] In a recent meta-analysis the risk in obstetric practice was estimated at 1:68,000.[7] In our patient, the haematoma presented with saddle anaesthesia, urinary and faecal incontinence and groin discomfort. The aetiology of the spinal haematoma in our patient is unclear, but it was not thought to be due to regional anaesthesia. She received prophylactic subcutaneous low molecular weight heparin for only five days postoperatively.

In conclusion, CIP is rare. When a patient with this condition presents in pregnancy we would recommend consultant-led care with an initial booking visit outlining the increased risk of tissue injury from the weight of the gravid uterus and the increased stress on the axial skeleton. Although the woman may not be aware of pain, she should be alert to any symptoms that are unusual and seek attention urgently. In cases where there is a history of undiagnosed fractures, a bone mineral density scan should be considered.

From an anaesthetic view, patients are unlikely to request epidural analgesia but routine regional anaesthesia is suggested for surgical intervention to minimize sensory input and processing. While there are no contraindications to vaginal birth everyone involved in the patient's care should be aware of the lack of pain sensation and its significance. We would also recommend vigilance throughout the post delivery period for gait disturbances and abnormal neurological signs.

DECLARATIONS

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